

*EMERGENT EQUIVALENCE RELATIONS BETWEEN
INTEROCEPTIVE (DRUG) AND EXTEROCEPTIVE (VISUAL) STIMULI*

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Conditional "if-then" relations between drug (interoceptive) stimuli and visual (exteroceptive) stimuli were taught to 4 normal humans. Interoceptive stimuli were the effects produced by 0.32 mg/70 kg triazolam (a prototypical benzodiazepine) and placebo (lactose-filled capsules); exteroceptive stimuli were black symbols on white flash cards. Following the training of the prerequisite conditional relations, tests of emergent relations were conducted between exteroceptive stimuli and between interoceptive and exteroceptive stimuli. Equivalence relations emerged immediately without explicit training for all 4 subjects. Accuracy of responding during the interoceptive-exteroceptive equivalence tests and subjects' self-reports showed consistent discrimination between the drug effects of triazolam and placebo. Finally, a generalization test assessed whether a novel visual stimulus presented in the context of the placebo (i.e., no drug) would generalize to visual stimuli belonging to the placebo stimulus class. All 3 subjects who completed this test reliably chose the visual stimuli belonging to the placebo class and not the visual stimuli belonging to the triazolam stimulus class. The development of equivalence relations between interoceptive and exteroceptive stimuli demonstrates that private and public stimulus events can emerge as members of the same equivalence class. Theoretical and clinical implications are discussed.

Key words: behavioral pharmacology, conditional discrimination, drug discrimination, matching to sample, private events, radical behaviorism, stimulus equivalence, stimulus generalization, triazolam, humans

The notion that the defining properties of stimuli are generic ones (Skinner, 1935)—that stimuli take on multiple functions for an organism and are best characterized by their function—has had important implications for the understanding of private events. Specifically, radical behaviorism posits that interoceptive (private) events can be conceptualized in much the same way as exteroceptive (public) events (Moore, 1980; Schnaitter, 1978; see also Skinner, 1953, 1957, 1974). As responses, they can be reinforced and punished; as discriminative stimuli (S^Ds), they can set the occasion for responding that may be public or private.

Empirical tests of private events as S^Ds are more numerous than are tests of private events as operant responses. Evidence of private events as S^Ds comes primarily from drug-discrimination research in behavioral pharmacology (Chait, Uhlenhuth, & Johanson, 1986; Over-

ton, 1984; Preston, Bigelow, Bickel, & Liebson, 1987; see also Girden & Culler, 1937; for an overview, see Overton, 1984; Schuster & Balster, 1977). The drug-discrimination procedure uses differential reinforcement to establish responding that comes under the discriminative control of the interoceptive effects of at least two drug conditions (e.g., morphine and placebo). For example, an active dose of drug or the control vehicle (placebo) is administered to a food-deprived animal that is then allowed to make a discrete choice response on one of two response manipulanda. When the drug has been administered, responses on the "drug" manipulandum result in the delivery of food, whereas responses on the other manipulandum do not result in food reinforcement; when saline is injected (i.e., placebo), reinforcement is contingent upon saline manipulandum responses. Similar procedures that produce similar results have also been employed in human drug-discrimination research (Bickel, Bigelow, Preston, & Liebson, 1989; Chait et al., 1986; Preston et al., 1987).

The drug-discrimination procedure is widely used in behavioral pharmacology and neuropharmacology, largely because of the concordance between the results of these studies and receptor-binding studies and because of the

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high degree of pharmacologic specificity (Overton, 1984; for an historical analysis see Branch, 1984; Stolerman & Shine, 1985). Drug-discrimination research provides considerable evidence that human and nonhuman animals can discriminate a range of psychoactive substances based on their interoceptive-stimulus effects (Holtzman, 1985; Overton, 1984). Thus, drug-discrimination research supports the notion that stimulus events "inside the skin" can serve discriminative functions (Skinner, 1953, 1974). A question that remains, however, is whether interoceptive stimuli can share membership in the same stimulus class as exteroceptive stimuli.

One method used to assess whether physically different stimuli can emerge as members of the same equivalence class is the stimulus equivalence procedure. In the prototypical procedure, a subject is shown a "sample" stimulus and a response is reinforced for choosing one of several nonidentical "comparison" stimuli (Sidman & Tailby, 1982). During training, conditional relations are taught by providing feedback as to whether each response is correct or incorrect (cf. Saunders, Saunders, Kirby, & Spradlin, 1988). On subsequent trials, the emergence of conditional relations is tested and no feedback is provided. This procedure is designed to test for the mathematical relations of reflexivity, symmetry, transitivity, which are defining properties of equivalence relations (Fields & Verhave, 1987; Sidman, 1990; Sidman & Tailby, 1982). For example, if the stimulus relations $A1 \rightarrow B1$ and $B1 \rightarrow C1$ were trained, with the first stimulus as the sample and the second stimulus as the correct comparison, the emergence of the following conditional relations could be assessed: (a) reflexivity (usually assumed; e.g., $A1 \leftrightarrow A1$), (b) symmetry (e.g., $B1 \rightarrow A1$), and (c) transitivity ($A1 \rightarrow C1$); a combined test for symmetry and transitivity can be used as a test for stimulus equivalence ($C1 \rightarrow A1$).

Emergent stimulus relations have been shown between visual stimuli (e.g., Sidman & Tailby, 1982), between visual and auditory stimuli (Saunders, Wachter, & Spradlin, 1988), and between visual and gustatory stimuli (Hayes, Tilley, & Hayes, 1988). The latter two studies demonstrate that stimuli impinging on different sensory modalities can nonetheless become members of the same equivalence

class. The present study integrated the stimulus equivalence procedure (e.g., Saunders, Wachter, & Spradlin, 1988; Sidman, 1971, 1990; Sidman & Cresson, 1973; Sidman & Tailby, 1982; Stromer & Osborne, 1982) with the drug-discrimination procedure to ascertain whether equivalence relations can emerge between interoceptive (drug) stimuli and exteroceptive (visual) stimuli in humans.

METHOD

Subjects, Stimuli, and Apparatus

Four normal adult volunteers (1 female and 3 males; aged 20 to 23 years), with a mean college education of 2.3 years, participated in the study. No subjects had experimental histories of learning conditional discriminations. Subjects gave informed consent and were in good health and without psychiatric disorder based on an interview conducted at the outset of the experiment.

The interoceptive stimuli were stimulus effects produced by 0.32 mg/70 kg triazolam (trade name Halcion®, a prototypical triazolobenzodiazepine) and placebo (lactose-filled capsules). Triazolam is used as a hypnotic and as an anxiolytic; active doses reduce self-reports of anxiety and increase self-reports of sedation (Oliveto, Bickel, Hughes, Higgins, & Fenwick, *in press*). The exteroceptive stimuli were black symbols on white flash cards presented by the experimenter (three stimuli per card). The black symbols were generated from the Cairo font on Apple Macintosh® computers. The visual stimuli were approximately 4 cm square and were equidistant from the perimeter of the white index cards (10 cm by 15 cm) and from one another (for comparison-stimuli cards). Training and testing of stimulus relations were conducted in a room that contained a card table, several chairs and desks, and a Commodore 64® microcomputer.

Procedure

Certain difficulties are inherent when using interoceptive stimuli in a matching-to-sample task. Among the most difficult is that interoceptive (drug) stimuli cannot easily be presented simultaneously (or even sequentially) as comparison stimuli. Literally, this would require presenting several interoceptively dis-

tinct stimuli simultaneously. This limitation is important because, when testing for equivalence, symmetry requires that each stimulus in any given symmetrical relation be tested as both a sample and a comparison stimulus. Not having the technology to administer distinct interoceptive stimuli (simultaneously) in an experimentally controlled and quantifiable fashion, we chose to use a procedure developed by Sidman and Tailby (1982, Figure 2; cf. Figure 1 in the present study). Sidman and Tailby (1982) faced a similar difficulty because they employed dictated Greek letters which also are difficult to present simultaneously as comparison stimuli.

General procedure. Subjects completed a total of approximately 15 sessions (one per day). In addition to the monetary compensation subjects received for participation in the study, they received some percentage of \$15.00 depending on their performance during training and testing. Sessions were defined as either *drug-visual* or *visual-visual* stimulus days (see below). Training and/or testing of conditional relations occurred in each session; relationships were explicitly taught during training trials (i.e., subjects received feedback—"correct" or "incorrect"—and monetary payment depending upon the accuracy of their responses). The emergence of symmetrical and transitive relations was assessed during test trials in which subjects received no feedback as to the accuracy of their responses.

A microcomputer was used for assessing subjects' self-reports of drug effects; subjects answered questions by responding on a console that contained three response keys that moved a cursor on the computer screen along a computer image of a visual analogue scale (VAS). Subjects could grade their response on the VAS, which was labeled "not at all" at one end of the scale and "very much" at the other end (range, 0 to 100).

Training and testing of stimulus relations were conducted with the subject and experimenter sitting and facing one another with a card table between them. Subjects responded by saying "left," "right," or "center" while pointing to either the left, right, or center stimulus on the comparison-stimuli card. Subsequently, the experimenter recorded the subject's response and provided feedback (on training trials only). Prior to being released

each drug day, subjects were told that they received either "Drug A" or "Drug B," which corresponded to placebo and triazolam; subjects were never informed of the actual drug or dose of drug they received.

Subjects were trained and tested independently (i.e., the 1st subject began and completed the study and was then followed by the 2nd subject, etc.) and had no contact with one another. (With the exception of Subjects AM and DA; Subject AM began the study when Subject DA had completed approximately 50% of the sessions. These 2 subjects were instructed not to discuss the experiment with one another at any time.)

The procedure was not automated. However, the experimenter was blind to the correct response on all test trials. That is, on test days, the experimenter simply recorded the subject's response (right, left, or center) and did not assess the accuracy of the subject's responses until completion of that portion of testing.

Sequence of conditions. The type of trials in each condition (training or testing) and the sample and comparison stimuli presented in each condition are shown in Table 1 (see also Figure 1). These conditions can be described in eight stages as follows:































































1. Pretest (Day 1). A pretest was conducted with each subject to familiarize them with the matching-to-sample procedure. During a 90-min session approximately 1 week prior to formally beginning the study, subjects were taught conditional relations between visual stimuli using the conditional discrimination procedure. Subjects were shown blue flash cards with symbols that differed from those used in the remainder of the study.

2. $A \rightarrow B$ and $A \rightarrow C$ training (Days 2–9). Either triazolam or placebo was administered. Two drug-visual stimulus relations were trained, on different days and in a random sequence, for both the triazolam stimulus and the placebo stimulus classes (i.e., triazolam-B1, triazolam-C1; placebo-B2, placebo-C2).

3. $A1 \rightarrow B1$ and $A1 \rightarrow C1$ tests (Day 10). Subjects were administered triazolam, and testing was conducted to ensure that the triazolam-B1 and triazolam-C1 relations were intact.

4. $A2 \rightarrow B2$ and $A2 \rightarrow C2$ tests (Day 11). The same procedure as on Day 10 was conducted, except placebo was administered (i.e.,

TABLE 1: SEQUENCE OF CONDITIONS

DAY	FUNCTION	STIMULUS CLASS	SYMBOLIC NOTATION				ACTUAL NOTATION			
			Sa:	Co+	Co-	Co-	Sa:	Co+	Co-	Co-
1	PRETEST		--	--	--	--	--	--	--	--
2/3/4/5	Train: A1->B1	1 (TRIAZOLAM)	A1:	B1	B2	A0	TRIAZ			
	or Train: A2->B2	2 (PLACEBO)	A2:	B2	B1	B0	PLAC			
6/7/8/9	Train: A1->C1	1 (TRIAZOLAM)	A1:	C1	C2	C0	TRIAZ			
	or Train: A2->C2	2 (PLACEBO)	A2:	C2	C1	D0	PLAC			
10	Test: A1->B1	1 (TRIAZOLAM)	A1:	B1	B2	?0	TRIAZ			?
	or Test: A1->C1	1 (TRIAZOLAM)	A1:	C1	C2	?0	TRIAZ			?
11	Test: A2->B2	2 (PLACEBO)	A2:	B2	B1	?0	PLAC			?
	or Test: A2->C2	2 (PLACEBO)	A2:	C2	C1	?0	PLAC			?
12(a)	Test: B1->C1	1 (TRIAZOLAM)	B1:	C1	B2	?0				?
	Test: C1->B1	1 (TRIAZOLAM)	C1:	B1	B2	?0				?
	Test: B2->C2	2 (PLACEBO)	B2:	C2	B1	?0				?
	Test: C2->B2	2 (PLACEBO)	C2:	B2	B1	?0				?
12(b)	Train: D1->C1	1 (TRIAZOLAM)	D1:	C1	D2	E0				
	Train: D2->C2	2 (PLACEBO)	D2:	C2	D1	F0				
12(c)	Test: C1->D1	1 (TRIAZOLAM)	C1:	D1	D2	?0				?
	Test: C2->D2	2 (PLACEBO)	C2:	D2	D1	?0				?
	Test: D1->B1	1 (TRIAZOLAM)	D1:	B1	C2	?0				?
	Test: B1->D1	1 (TRIAZOLAM)	B1:	D1	C2	?0				?
	Test: D2->B2	2 (PLACEBO)	D2:	B2	C1	?0				?
	Test: B2->D2	2 (PLACEBO)	B2:	D2	C1	?0				?
13/14	Test: A1->D1	1 (TRIAZOLAM)	A1	D1	D2	?0	TRIAZ			?
	or Test: A2->D2	2 (PLACEBO)	A2	D2	D1	?0	PLAC			?

Sa = Sample, Co+ = Correct Comparison, Co- = Incorrect Comparison, ? = stimulus varied within subject

placebo-B2 and placebo-C2 relations were tested).

5. B ↔ C tests (Day 12, Condition a). No drug capsules were administered. Equivalence relations were assessed separately for the two visual stimuli paired with triazolam and the two visual stimuli paired with placebo. Equivalence was demonstrated for the triazolam

stimulus class if subjects chose the B1 comparison stimulus when C1 was presented as the sample stimulus, and vice versa; equivalence was demonstrated for the placebo stimulus class if subjects chose the B2 comparison stimulus when C2 was presented as the sample stimulus, and vice versa.

6. D → C training (Day 12, Condition b).

No drug capsules were administered. An additional member (D1 and D2, respectively, for the triazolam and placebo stimulus classes) was trained to a member (C1 and C2, respectively) of its respective stimulus class.

7. $C \rightarrow D$, $B \leftrightarrow D$ tests (Day 12, Condition c). No drug capsules were administered. Visual-visual equivalence relations were assessed, one at a time. In total, this included a test of four new relations.

8. $A \rightarrow D$ tests (Days 13 and 14). Either triazolam or placebo was administered. The equivalence relation between the stimulus effect of the drug (triazolam or placebo) and the third visual stimulus was assessed (D1 or D2).

Drug-visual stimuli days. Upon arrival at the laboratory, behavioral and physiological baseline measures were taken for safety purposes, followed by the administration of either drug or placebo via two blue opaque capsules. Training and/or testing of stimulus relations were conducted three times postdrug (60, 75, and 90 min after drug ingestion). This consisted of presenting the subject with three comparison-stimuli cards, one at a time, at each of the three time points; that is, subjects responded to a total of nine comparison cards on drug-visual testing or training days (nine trials). However, on Days 10 and 11 (see Table 1), two tests were conducted during the nine trials; consequently, four of the nine comparison-stimuli cards were presented to test one of the two stimulus relations and five cards were presented to test the other stimulus relation (presented in a mixed sequence). The order of the three visual stimuli on the cards varied in a random sequence (see below). The command "match the drug stimulus with the visual stimulus," was presented with the first comparison card at each time point.

Immediately prior to the training or testing at each time point, subjects provided self-reports of drug (or placebo) effects and responded to the questions: "How much is the drug like Drug A?" and "How much is the drug like Drug B?" by responding on a computer VAS. On the first drug day, subjects were instructed to "ignore these two questions until they had received both Drug A and Drug B."

Visual-visual stimuli day. On this day, no drug was administered; training or testing occurred 60 min after the subject's arrival at the laboratory and subsequently at 10-min inter-

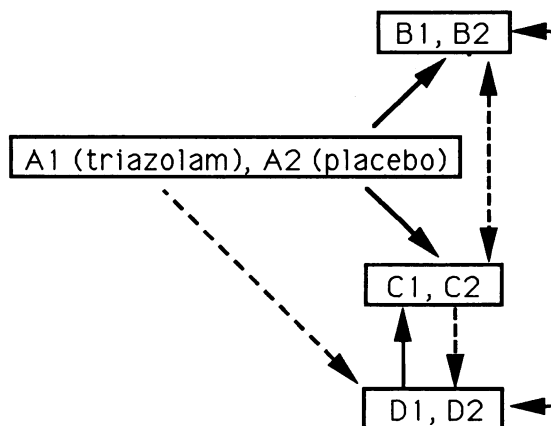


Fig. 1. A flow diagram of the stimulus equivalence procedure used in this experiment. Interceptive (drug) stimuli are denoted by drug name (i.e., triazolam and placebo) and by letter-number combinations (e.g., A1); visual stimuli are denoted by letter-number combinations (e.g., B1). Visual stimuli belonging to Classes 1 and 2 correspond with the interoceptive stimuli (triazolam and placebo, respectively) (see Table 1 for actual visual stimuli). Solid arrows represent trained relations and dashed arrows represent tested relations. The stimulus shown at the start of each arrow is a sample stimulus, whereas the stimulus at the end of each arrow is the correct comparison stimulus.

vals until all training and testing conditions were completed. Sample- and comparison-stimuli cards were presented to the subject along with the command "match the visual stimulus with the visual stimulus." Nine trials were conducted for each training and testing condition.

Generalization test. On Day 15 (not shown in Table 1), no drug was administered; a generalization test was conducted that examined which stimuli—placebo-visual stimuli or triazolam-visual stimuli—the subject would choose when presented with a sample (visual) stimulus that had no previous relation with the visual stimuli from either of the two equivalence classes. That is, tests were conducted to assess whether equivalence relations might emerge as a consequence of stimulus generalization via physical similarity.

The procedure was as follows. First, a new visual stimulus (a black "+" symbol, denoted below as Stimulus F), similar in size to the visual stimuli from the two equivalence classes presented previously, was trained as a correct comparison to a second new stimulus (a 2-cm red colored square, denoted below as Stimulus

Table 2
Percentage correct in testing.

	Subject			
	MO	DA	AM	SM
Percentage correct in testing (overall)	100	100	98.8	100
Percentage correct on Day 12				
Condition <i>a</i>	100	100	100	100
Condition <i>b</i>	100	100	100	100
Condition <i>c</i>	100	100	94.4	100
Percentage correct on Day 13	100	100	100	100
Day 14	100	100	100	100

E). This can be expressed as $E \rightarrow F$ training. The "red square" stimulus was used because, like the interoceptive stimuli, it differed considerably from all the other visual stimuli in the experiment. Second, after training the $E \rightarrow F$ relation, Stimulus F was presented as the sample stimulus and two visual stimuli, one from each potential equivalence class, were presented as comparison stimuli. Because these tests were conducted using the three visual stimuli (i.e., B, C, D) from each of the two equivalence classes, these tests can be expressed as $F \rightarrow B$, $F \rightarrow C$, and $F \rightarrow D$ tests. For example, a subject would be shown Stimulus F as the sample stimulus and would choose between B1 and B2 as the comparison stimulus. One of the three sets of comparison stimuli was presented at each of the three time points spaced 10 min apart, in a mixed order across subjects; the stimuli locations during the three trials at each time also varied randomly.

Comparison stimuli. Several precautions were taken when determining the incorrect comparison stimuli to be presented along with the correct comparison stimulus. These measures were used to ensure that the subject was unable to respond correctly by exclusion, and to ensure that one incorrect stimulus was not highly correlated with a specific correct comparison stimulus. Although only two stimulus classes were trained and tested, three comparison stimuli were presented on all training and testing trials (except on Day 15) to decrease the probability of correct responding by chance (see Sidman, 1987). More specifically, the correct comparison stimulus was presented along with one comparison stimulus from the other drug class (placebo or triazolam) and one comparison

stimulus that was never correct ("dummy" stimuli, shown as Stimulus Class 0 in Table 1). The dummy stimulus that was presented during training and testing trials was varied across trials. For example, during any nine training or testing trials one of two dummy stimuli were presented (randomly) along with the correct comparison and a comparison from the other drug class. The right column in Table 2 shows the incorrect comparison stimuli that were never correct. In summary, the dummy stimuli were presented in the manner described above to ensure that (a) subjects could not respond solely by exclusion (i.e., three alternatives require the subject who never chooses one stimulus to still make a choice between the two remaining stimuli) and (b) correct responses could not be discriminated on the basis of the "never correct" stimulus, because the "never correct" stimuli were never consistently presented with any one sample stimulus.

RESULTS

Results are discussed in the sequence in which they occurred. First, via the pretest that was conducted to familiarize the subjects with the matching-to-sample procedure (Day 1), all 4 subjects readily demonstrated the ability to develop equivalence relations between exteroceptive stimuli; detailed results are not presented.

Next, on the first drug day for either placebo or triazolam, subjects acquired the discrimination via trial and error, and errors across subjects ranged from zero to two (of a possible nine). Following 1 day of training for each of the two drug-visual stimulus relations, subjects made no further errors in the conditional discriminations during training and earned the full monetary bonus on each day (\$15.00).

Next, during tests of whether the drug-visual relations for the placebo and the triazolam classes were intact (Days 10 and 11), subjects responded without errors. This result is consistent with the finding that—across all drug days—subjects made no errors in the drug discrimination other than during their first exposure to triazolam and placebo.

The accuracy of the discrimination between triazolam and placebo was substantiated via the VAS scores derived from the "How much like Drug A?" and "How much like Drug B?" questions. These data are shown in Figure 2.

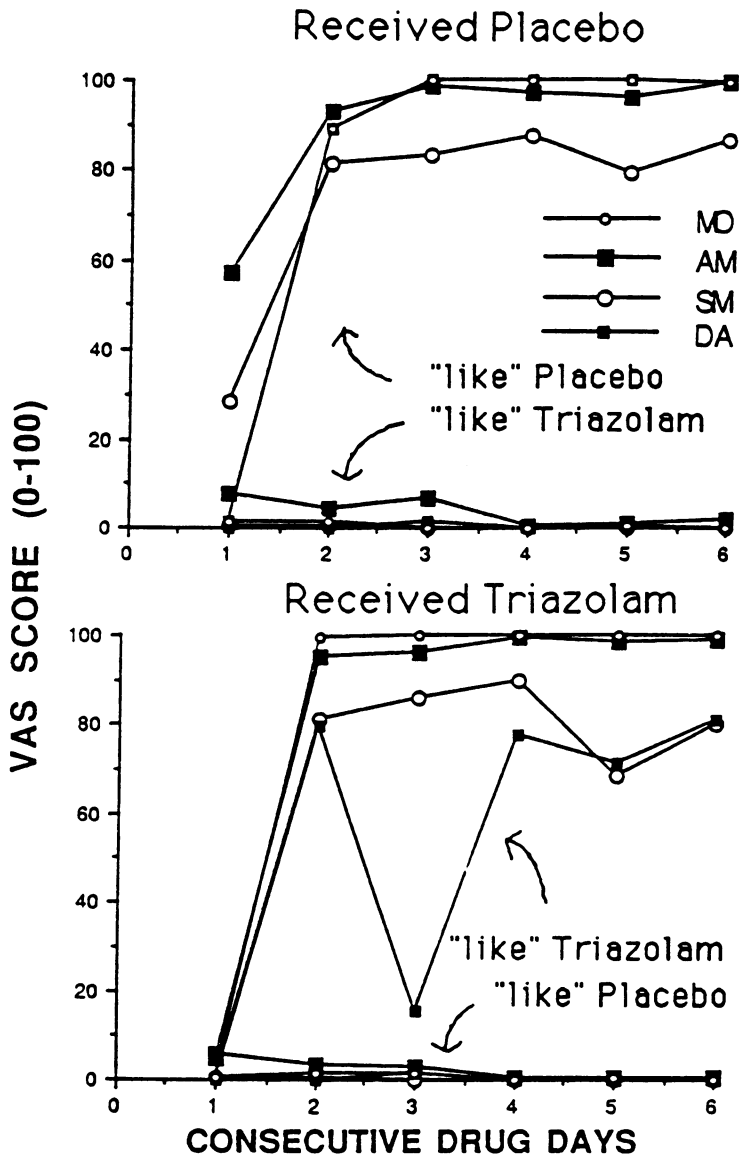


Fig. 2. Mean visual analogue scale (VAS) scores (range, 0 to 100) are shown for all 4 subjects for the "how much like Drug A?" and "how much like Drug B?" questions when placebo was administered (top panel) and when triazolam was administered (lower panel) as a function of consecutive placebo and triazolam days, respectively (means represent the VAS scores at the three time points postdrug). If "Drug A" referred to placebo, then "Drug B" referred to triazolam, and vice versa. See text for details.

Mean VAS scores (range, 0 to 100) are shown for all 4 subjects for these two questions when placebo was administered and when triazolam was administered as a function of consecutive placebo and triazolam days, respectively (means were derived from VAS scores at the three time points postdrug). (Note that if "Drug A" referred to placebo, "Drug B" referred to triazo-

lam, and vice versa.) Subjects reliably reported that the drug was "more like placebo" than "triazolam" when administered placebo, with the discrimination improving as a function of consecutive placebo days. Subject SM's responding produced the lowest difference score (range, 80 to 88), whereas the difference score for the last three placebo days for Subjects MO

and DA was the maximum (i.e., 100). A similar effect occurred for triazolam (Figure 2).

The tests for equivalence relations between two exteroceptive stimuli, and between an interoceptive and an exteroceptive stimulus, occurred in all 4 subjects (see Table 2). When testing for the emergence of symmetrical and equivalence relations (Days 12 to 14), 3 of the 4 subjects' responses were 100% "correct" (i.e., in conformity with equivalence) and 1 subject made one incorrect response. The incorrect response was made by Subject AM on the second of nine trials during the C2 \rightarrow D2 symmetry test (Day 12, Condition *c*); Subject AM's response accuracy on Day 12 (Condition *c*) was 94.4% correct (17 of 18 trials correct; 6 tests by 3 trials = 18 total trials). Overall, emergence of equivalence relations was demonstrated for the visual-visual relations, B \leftrightarrow D, and for drug-visual relations, A \rightarrow D (see Table 2). The development of equivalence relations between interoceptive and exteroceptive stimuli indicates that subjects accurately discriminated between triazolam and placebo (Figure 2).

On the generalization test (Day 15), the 3 subjects who completed this condition (AM, DA, SM) consistently responded to the stimuli belonging to the placebo stimulus class. That is, during the test trials that included a visual stimulus from both stimulus classes, subjects chose the visual stimuli from the placebo class on all nine trials.

DISCUSSION

In summary, the present study contains three significant findings. First, interoceptive-exteroceptive stimulus relations can be learned by human subjects via the stimulus equivalence procedure. This is a systematic replication of previous research in human drug discrimination (Bickel *et al.*, 1989; Preston *et al.*, 1987), and demonstrates that triazolam can serve as a discriminative stimulus in humans. Second, as a consequence of these learned relations (via training), interoceptive-exteroceptive stimulus equivalence relations can emerge without explicit training. To our knowledge, this has not been demonstrated previously. This finding also extends previous research demonstrating equivalence relations with stimuli that impinge on different sensory modalities (e.g., Hayes *et al.*, 1988). Third, when a new stimulus was presented on a nondrug day, sub-

jects chose the visual stimuli that had been paired with the same interoceptive stimuli (i.e., placebo). This phenomenon of generalization via physical similarity is consistent with the possibility that novel exteroceptive stimuli can enter into equivalence classes by virtue of their common interoceptive stimulus effects. The present study, however, did not include conditions (e.g., no experience with Stimuli E or F prior to the test, or tests with the B, C, or D stimuli as samples and F as the comparison) that would allow a more definitive conclusion.

The finding that equivalence classes can contain interoceptive and exteroceptive stimuli strengthens Skinner's notion of the generic nature of the concepts of stimulus and response (Skinner, 1935). That is, this study lends further support to the idea that stimuli "inside the skin" can acquire and exert stimulus control over responding in apparently the same manner as exteroceptive stimuli. However, these results go beyond previous research on discriminated responding by providing a mechanism for explaining how interoceptive stimuli can transfer their stimulus control function to environmental stimuli that were never explicitly paired with those interoceptive stimuli (i.e., emerge as members of the same equivalence class). The importance of equivalence classes of this type is, in part, that they provide an empirical framework for studying verbal repertoires that seemingly relate to private events. (See Lubinski & Thompson, 1987, for an interesting demonstration, in pigeons, of how interoceptive events can serve as S^Ds, be named, and in turn be communicatively transmitted to other individuals; see also Skinner, 1945, 1957.) Consider, for example, a child's verbal stimulus equivalence class containing "it aches" and "it hurts" merging for the first time with the interoceptive stimulus equivalence class containing stimuli associated with an earache and a headache. When the two classes are merged by teaching the child to say "it aches" when he or she has an earache, the child might then make any of three emergent responses: "it aches" when having a headache, "it hurts" when having a headache, and "it hurts" when having an earache.

Lacking in the above example is a complete explanation of how equivalence relations develop between stimuli occurring in the natural environment. That is, it is unlikely that equivalence relations always develop between stimuli in the natural environment in the same way

they do during matching-to-sample conditional discrimination training (i.e., explicitly reinforced conditional discriminations). The third finding—that novel exteroceptive stimuli may generalize to exteroceptive stimuli that have been paired with the same interoceptive stimuli (i.e., the absence of any drug effect or placebo)—if true, suggests that stimuli may enter into equivalence relations with other stimuli via stimulus generalization. This finding is supported by a recent study demonstrating multiple sources of entry into equivalence classes (Fields, Reeve, Adams, & Verhave, 1991). Fields et al., using normal adult subjects, demonstrated that stimuli similar but not identical to a member of a stimulus equivalence class generalized to other members of that equivalence class. As a result, Fields et al. concluded that “the development of complex naturally occurring categories may be accounted for by the combined effects of equivalence class formation and stimulus generalization” (p. 311).

If new equivalence relations can emerge as a function of stimulus generalization, the finding that interoceptive and exteroceptive stimuli can share membership in an equivalence class has important clinical implications. Specifically, the present findings, along with the findings reported by Fields et al. (1991), suggest a potential mechanism for explaining how clinically significant responses come under complex stimulus control; that is, how environmental “precipitators” or “triggers” (that subjects are often unaware of) set the occasion for responding (see Margraf, Taylor, Ehlers, Roth, & Agras, 1987; Street, Craske, & Barlow, 1989). For example, Street et al. suggested that the distinction between cued and uncued (“out of the blue”) panic attacks may be somewhat false in that “cues outside the individual’s awareness most likely exist” (p. 189). This suggestion raises an interesting possibility: Perhaps stimulus control could transfer from the more clearly identifiable cues, such as those present in the “classic phobic situation,” to less salient stimuli that exist in environments paired with panic attacks. Assuming that there are similar interoceptive stimuli associated with panic attacks and normal anxiety experienced by most people, the possibility exists that as a result of generalization, equivalence relations might emerge between the stimuli that facilitate the onset of panic attacks and those stimuli that increase anxiety. That

is, stimulus generalization as a source of entry into equivalence classes provides a mechanism for explaining how exteroceptive stimuli paired previously with interoceptive stimuli might increase the number of stimuli controlling clinically significant behavioral problems such as panic attacks.

Examples of stimulus control over types of behavior that have interoceptive components have been suggested in research on substance abuse (e.g., conditioned drug taking, conditioned withdrawal, conditioned tolerance, drug reinstatement; Bickel & Kelly, 1988; O’Brien, 1975; O’Brien, Childress, McLellan, Ehrman, & Ternes, 1988; O’Brien, Testa, O’Brien, Brady, & Wells, 1977; Siegel, 1978, 1988), anxiety disorders (e.g., generalized anxiety, situational anxiety, panic attacks, worrying; Barlow et al., 1985; Borkovec, Wilkinson, Folsensbee, & Lerman, 1983; Margraf et al., 1987), eating disorders (e.g., dietary restraint; Ruderman, 1986), and epilepsy (Verduyn, Stores, & Missen, 1988). Despite these reports, the development, complexity, and pervasiveness of these controlling-stimulus relations are not well understood (Street et al., 1989). Indeed, prior to this study, no mechanism had been proposed that was capable of explaining how emergent stimulus control develops between interoceptive and exteroceptive stimuli. Given the paucity of research investigating stimulus control over clinically relevant behavior (see Bickel & Kelly, 1988), the present findings attest to the value and need for more explorative research on emergent stimulus control in these areas.

REFERENCES

- Barlow, D. H., Vermilyea, J., Blanchard, E. B., Vermilyea, B. B., Di Nardo, P. A., & Cerny, J. A. (1985). The phenomenon of panic. *Journal of Abnormal Psychology*, *94*, 320–328.
- Bickel, W. K., Bigelow, G. E., Preston, K. L., & Liebson, I. A. (1989). Opioid drug discrimination in humans: Stability, specificity and relation to self-reported drug effect. *Journal of Pharmacology and Experimental Therapeutics*, *251*, 1053–1063.
- Bickel, W. K., & Kelly, T. H. (1988). The relationship of stimulus control to the treatment of substance abuse. In B. A. Ray (Ed.), *Learning factors in substance abuse* (National Institute on Drug Abuse Monograph 84, pp. 122–140). Washington, DC: U.S. Government Printing Office.
- Borkovec, T. D., Wilkinson, L., Folsensbee, R., & Lerman, C. (1983). Stimulus control applications to the study of worry. *Behaviour Research and Therapy*, *21*, 247–251.
- Branch, M. N. (1984). Rate dependency, behavioral

- mechanisms, and behavioral pharmacology. *Journal of the Experimental Analysis of Behavior*, **42**, 512-522.
- Chait, L. D., Uhlenhuth, E. H., & Johanson, C. E. (1986). The discriminative stimulus and subjective effects of *d*-amphetamine, phенmetrazine and fenfluramine in humans. *Psychopharmacology* (Berlin), **89**, 301-306.
- Fields, L., Reeve, K. F., Adams, B. J., & Verhave, T. (1991). Stimulus generalization and equivalence classes: A model of natural categories. *Journal of the Experimental Analysis of Behavior*, **55**, 305-312.
- Fields, L., & Verhave, T. (1987). The structure of equivalence classes. *Journal of the Experimental Analysis of Behavior*, **48**, 317-332.
- Girden, E., & Culler, E. (1937). Conditioned responses in curarized striate muscle in dogs. *Journal of Comparative Psychology*, **23**, 261-274.
- Hayes, L. J., Tilley, K. J., & Hayes, S. C. (1988). Extending equivalence class membership to gustatory stimuli. *Psychological Record*, **38**, 473-482.
- Holtzman, S. G. (1985). Discriminative stimulus properties of opioids that interact with mu, kappa, and PCP/sigma receptors. In L. S. Seiden & R. L. Balster (Eds.), *Behavioral pharmacology: The current status* (pp. 131-147). New York: Alan R. Liss.
- Lubinski, D., & Thompson, T. (1987). An animal model of the interpersonal communication of interoceptive (private) states. *Journal of the Experimental Analysis of Behavior*, **48**, 1-16.
- Margraf, J., Taylor, B., Ehlers, A., Roth, W. T., & Agras, S. (1987). Panic attacks in the natural environment. *Journal of Nervous and Mental Disorders*, **175**, 558-565.
- Moore, J. (1980). On behaviorism and private events. *Psychological Record*, **30**, 459-475.
- O'Brien, C. P. (1975). Experimental analysis of conditioning factors in human narcotic addiction. *Pharmacology Review*, **27**, 535-543.
- O'Brien, C. P., Childress, A. R., McLellan, A. T., Ehrman, R., & Ternes, W. J. (1988). Types of conditioning found in drug-dependent humans. In B. A. Ray (Ed.), *Learning factors in substance abuse* (National Institute on Drug Abuse Monograph 84, pp. 44-61). Washington, DC: U.S. Government Printing Office.
- O'Brien, C. P., Testa, T., O'Brien, T. J., Brady, J. P., & Wells, B. (1977). Conditioned narcotic withdrawal in humans. *Science*, **195**, 1000-1002.
- Oliveto, A. H., Bickel, W. K., Hughes, J. R., Higgins, S. T., & Fenwick, J. W. (in press). Triazolam as a discriminative stimulus in humans. *Drug and Alcohol Dependence*.
- Overton, D. A. (1984). State dependent learning and drug discrimination. In L. L. Iverson, S. D. Iverson, & S. H. Snyder (Eds.), *Handbook of psychopharmacology* (pp. 59-69). New York: Plenum Press.
- Preston, K. L., Bigelow, G. E., Bickel, W., & Liebson, I. E. (1987). Three-choice drug discrimination in opioid-dependent humans: Hydromorphone, naloxone, and saline. *Journal of Pharmacology and Experimental Therapeutics*, **243**, 1002-1009.
- Ruderman, A. J. (1986). Dietary restraint: A theoretical and empirical review. *Psychological Bulletin*, **99**, 247-262.
- Saunders, R. R., Saunders, K. J., Kirby, K. C., & Spradlin, J. E. (1988). The merger and development of equivalence classes by unreinforced conditional selection of comparison stimuli. *Journal of the Experimental Analysis of Behavior*, **50**, 145-162.
- Saunders, R. R., Wachter, J., & Spradlin, J. E. (1988). Establishing auditory stimulus control over an eight-member equivalence class via conditional discrimination procedures. *Journal of the Experimental Analysis of Behavior*, **49**, 95-116.
- Schnaitter, R. (1978). Private causes. *Behaviorism*, **6**, 1-12.
- Schuster, C. R., & Balster, R. L. (1977). The discriminative properties of drugs. In T. Thompson & P. B. Dews (Eds.), *Advances in behavioral pharmacology* (Vol. 1, pp. 86-134). New York: Academic Press.
- Sidman, M. (1971). Reading and auditory-visual equivalences. *Journal of Speech and Hearing Research*, **14**, 5-13.
- Sidman, M. (1987). Two choices are not enough. *Behavior Analyst*, **22**, 11-18.
- Sidman, M. (1990). Equivalence relations: Where do they come from? In D. E. Blackman & H. Lejeune (Eds.), *Behaviour analysis in theory and practice: Contributions and controversies* (pp. 93-114). East Sussex, England: Erlbaum.
- Sidman, M., & Cresson, O., Jr. (1973). Reading and cross-modal transfer of stimulus equivalences in severe retardation. *American Journal of Mental Deficiency*, **77**, 515-523.
- Sidman, M., & Tailby, W. (1982). Conditional discrimination vs. matching to sample: An expansion of the testing paradigm. *Journal of the Experimental Analysis of Behavior*, **37**, 5-22.
- Siegel, S. (1978). Tolerance to the hypothermic effect of morphine in the rat is a learned response. *Journal of Comparative and Physiological Psychology*, **92**, 1137-1149.
- Siegel, S. (1988). Drug anticipation and the treatment of dependence. In B. A. Ray (Ed.), *Learning factors in substance abuse* (National Institute on Drug Abuse Monograph 84, pp. 1-28). Washington, DC: U.S. Government Printing Office.
- Skinner, B. F. (1935). The generic nature of stimulus and response. *Journal of General Psychology*, **12**, 40-65.
- Skinner, B. F. (1945). The operational analysis of psychological terms. *Psychological Review*, **52**, 270-277.
- Skinner, B. F. (1953). *The science of human behavior*. New York: Macmillan.
- Skinner, B. F. (1957). *On verbal behavior*. New York: Appleton-Century-Crofts.
- Skinner, B. F. (1974). *About behaviorism*. New York: Knopf.
- Stolerman, I. P., & Shine, P. J. (1985). Trends in drug discrimination research analysed with a cross-indexed bibliography, 1982-1983. *Psychopharmacology* (Berlin), **86**, 1-11.
- Street, L. L., Craske, M. G., & Barlow, D. H. (1989). Sensations, cognitions and the perception of cues associated with expected and unexpected panic attacks. *Behaviour Research and Therapy*, **27**, 189-198.
- Stromer, R., & Osborne, J. G. (1982). Control of adolescents' arbitrary matching-to-sample by positive and negative stimulus relations. *Journal of the Experimental Analysis of Behavior*, **37**, 329-348.
- Verduyn, C. M., Stores, G., & Missen, A. (1988). A survey of mothers' impressions of seizures precipitants in children with epilepsy. *Epilepsy*, **29**, 251-255.

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